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Bithiophene with Winding Vine-shaped Molecular Asymmetry. Preparation, Structural Characterization, and Enantioselective Synthesis

Yuka Toyomori,[1] Satoru Tsuji,[1] Shinobu Mitsuda,[1] Yoichi Okayama,[1] Shiomi Ashida,[1] Atsunori Mori,*[1] Toru Kobayashi,[2] Yuji Miyazaki,[2] Tsuyoshi Yaita,[2] Sachie Arae,[3] Tamotsu Takahashi,[3] and Masamichi Ogasawara*[3,†]

[1]Department of Chemical Science and Engineering, Kobe University, 1-1 Rokkodai, Nada, Kobe, Hyogo 657-8501

[2]Quantum Beam Science Directorate Japan Atomic Energy Agency, 1-1-1 Koto, Sayo-cho, Sayo-gun, Hyogo 679-5148

[3]Institute for Catalysis, Hokkaido University, Kita21, Nishi10, Kita-ku, Sapporo, Hokkaido 001-0021

E-mail: amori@kobe-u.ac.jp, ogasawar@tokushima-u.ac.jp

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Atsunori Mori

Atsunori Mori was born in Japan in 1959 and he received B.S. (1982), M.S. (1984), and Ph.D. (1987) degrees from Nagoya University under the direction of Professor Hisashi Yamamoto. After postdoctoral study in U. C. Berkeley with Peter Vollhardt (1987–1988), he started his academic carreer as an Assistant Professor at the University of Tokyo (1988) and Japan Advanced Institute of Science and Technology (1993). He was appointed as an Associate Professor in 1995 at Chemical Resources Laboratory of Tokyo Institute of Technology. Since 2005, he has been Professor at the Graduate School of Engineering, Kobe University.

Masamichi Ogasawara

Masamichi Ogasawara was born in Japan in 1966. He obtained the bachelor, master, and doctor degrees from the University of Tokyo in 1989, 1991, and 1994, respectively. After the three years postdoctoral spell in USA (1994–1996 with Prof. K. G. Caulton at Indiana University; 1996–1997 with Prof. T. J. Marks at Northwestern University), he joined the Department of Chemistry, Kyoto University as an assistant professor. In 2002, he moved to Catalysis Research Center of Hokkaido University as an associate professor. Since 2016, he has been a full professor at Graduate School of Science and Technology, Tokushima University.

Abstract

Preparation of 2,2′-bithiophene derivatives bearing ω-alkenyl groups at the 3,3′-positions and ring-closing metathesis reactions of the obtained compound were performed. The reaction of bithiophene bearing 3-butenyl substituents **1** with 5 mol % Grubbs 1st generation catalyst underwent ring-closing metathesis (RCM) to afford the cyclized product **7** showing winding vine-shaped molecular asymmetry in up to 88% yield. Enantioselective RCM was also achieved by the use of chiral Schrock–Hoveyda molybdenum-alkylidene catalyst in up to 87% ee.

1. Introduction

Design of novel organic compounds showing molecular asymmetry attracts much attention out of topochemical interest[1] as well as application of such compounds as functional organic molecules particularly as asymmetric catalysts.[2] We have recently reported that ring-closing metathesis (RCM)[3] of a bisimidazole derivative bearing *N*-butenyl substituents leads to macrocyclic *E*-olefin and the thus cyclized product shows a novel class of molecular asymmetry.[4] The chirality in this unique molecule could be viewed in multiple ways as axial, planar, or helical chirality, and we have proposed the term "winding vine-shaped molecular asymmetry" for this molecular asymmetry. We have also been successful in enantioselective preparation of such compounds of molecular asymmetry using a chiral molybdenum-alkylidene catalyst.[5] Our further concern turned to the design of other heterobiaryls showing related molecular asymmetry. Since we have been interested in developing C–H functionalization reactions of five-membered heteroaromatic compounds[6] representative as thiophene derivatives[7] directed to advanced organic materials, it is intriguing to study if preparation of such vine-shaped compounds is possible in thiophene derivatives.[1] Herein, we report concise preparation of 2,2′-bithiophene derivatives bearing ω-alkenyl substituents at the 3- and 3′-positions in the thiophene rings and ring-closing metathesis of the thus obtained compounds lead-

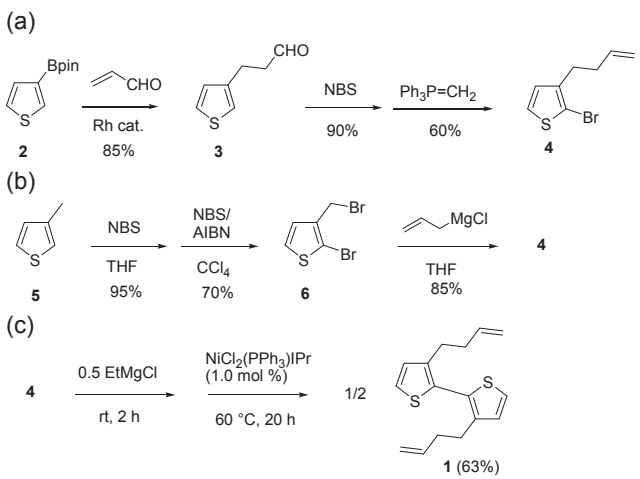
† Present address: Graduate School of Science and Technology, Tokushima University, 2-1 Minamijyousanjima-cho, Tokushima 770-8506

ing to bithiophenes with winding vine-shaped molecular asymmetry. Transformation of the cyclized bithiophene and their enantioselective preparation by molybdenum-catalyzed asymmetric ring-closing metathesis are also studied.[8]

2. Results and Discussion

Thiophene derivative **1** bearing ω-olefinic substituents at the 3- and 3′-positions was synthesized as shown in the following pathways: the reaction of (3-thienyl)boronate **2** with acrolein in the presence of a rhodium catalyst afforded aldehyde **3**.[9] Subsequent bromination at the 2-position of thiophene and Wittig methylenation lead to 2-bromo-3-(3-buten-1-yl)thiophene **4** (Scheme 1a). Bromothiophene **4** was also obtained from 3-methylthiophene (**5**) by sequential cationic and radical bromination reactions of **5** both with NBS to afford 2-bromo-3-bromomethylthiophene (**6**) in 95% and 70% yields, respectively. Treatment of **6** with allyl Grignard reagent leads to **4** (85%), whose protocol has also been applied to the monomer synthesis of polythiophene with extremely high solubility in hydrocarbons (Scheme 1b).[10] Obtained 3-substituted bromothiophene **1** was subjected to dimerization of the thienylmagnesium species formed by halogen–metal exchange with a half equivalent of EtMgCl followed by palladium-catalyzed cross coupling with the remaining **4**, to afford **1** in 63% yield. (Scheme 1c) Preparation of **1** was alternatively carried out by oxidative homocoupling, which was performed by the reaction of the metalated thiophene with $CuCl_2$ (70%).[11]

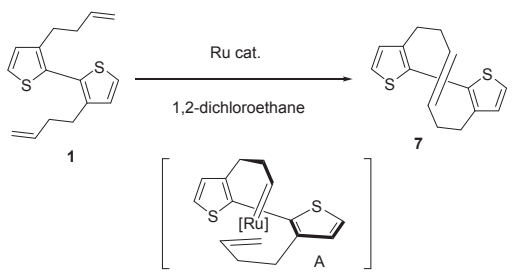
The obtained bithiophene **1** was subjected to the ring-closing metathesis (RCM) with a ruthenium catalyst as shown in Scheme 2. In RCM of bisimidazole derivatives[4] the reaction using Grubbs 2nd generation catalyst[12] in the presence of a Lewis acid $Ti(OiPr)_4$ as an additive has been effective,[13] however, the reaction of bithiophene derivative **1** proceeded smoothly without Lewis acid to give the cyclized product **7** in 67% yield. The absence of imino nitrogen may have avoided poisoning of the ruthenium catalyst facilitating the smooth reaction of the ruthenium complex with a terminal olefin leading to alkylidene ruthenium complex **A**. Thus, thiophene–thiophene bond rotation would lead to favorable intramolecular metathesis reaction. Cooling the reaction to room temperature with Grubbs 2nd generation catalyst resulted in no reaction, while the reaction was found to proceed at room temperature with Grubbs 1st generation catalyst[12b,14] within a shorter reaction period (1 h, 77%) suggesting that bithiophene **1** was much more reactive compared with the bisimidazole analog. The reaction of **1** under much higher dilution (0.05 to 0.025 M) improved the yield to 88%. The results are summarized in Table 1.



Scheme 1. Preparation of bithiophene RCM precursor.

Measurement of the mass spectrum of the metathesis product supported formation of the cyclized product **7** with liberation of ethylene from **1**. The ^1H NMR spectrum of **7** also supports formation of macrocyclic *E*-olefin structure to bring about a remarkable shift of the vinylic proton signal (5.8 ppm) to lower frequency induced by the placement of the corresponding hydrogen atom in the deshielded region of the ring current of thiophene. Measurement of UV–vis spectra of **7** and the metathesis precursor **1** suggested less π-conjugation between the thiophenes in **7** after the ring closure to result in twisting of the dihedral angle of the two thiophene rings by the formation of the olefinic 10-membered ring. HPLC analysis of **7** was carried out with a chiral column DAICEL Chiralpak IF to observe separation of the enantiomers with hexane as an eluent (Figure 1a).

Figure 1b shows an ORTEP diagram of X-ray structure analysis of *rac*-**7** showing the 10-membered macrocyclic *E*-olefin involving bithiophene.[15] Similar to the case of bisimidazole the crystal structure was composed of an enantiopair of (*R*) and (*S*) isomers. It was found that the dihedral angle between the thiophene rings was 74.0°. Comparing with that of imidazole (47.8°)[4a] bithiophene exhibited a more twisted structure because the carbon atom bearing a substituent was sp^2-hybridized



Scheme 2. Ring-closing metathesis of bithiophene **1** leading to macrocyclic olefin with winding vine-shaped molecular asymmetry.

Table 1. Ring-closing metathesis of bithiophene 1[a)]

Catalyst[b)] (mol %)	Temp (°C)	Time (h)	Yield of **7** (%)
Grubbs 2nd (5)	80	24	67
Grubbs 2nd (5)	rt	24	0
Grubbs 1st (5)	80	24	70
Grubbs 1st (5)[c)]	rt	1	77
Grubbs 1st (10)[d)]	rt	5	88

a) Unless noted, the reaction was carried out with **1** in 1,2-dichloroethane (0.05 M) under a nitrogen atmosphere. b) Grubbs 2nd: $RuCl_2(=CHPh)(PCy_3)SIMes$; Grubbs 1st: $RuCl_2(=CHPh)(PCy_3)_2$. c) The reaction was carried out with dichloromethane (0.05 M) as a solvent. d) The reaction with dichloromethane (0.025 M).

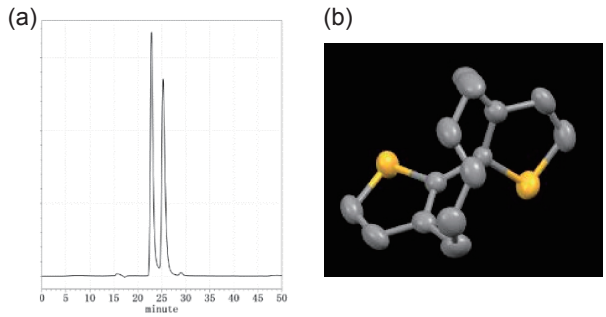
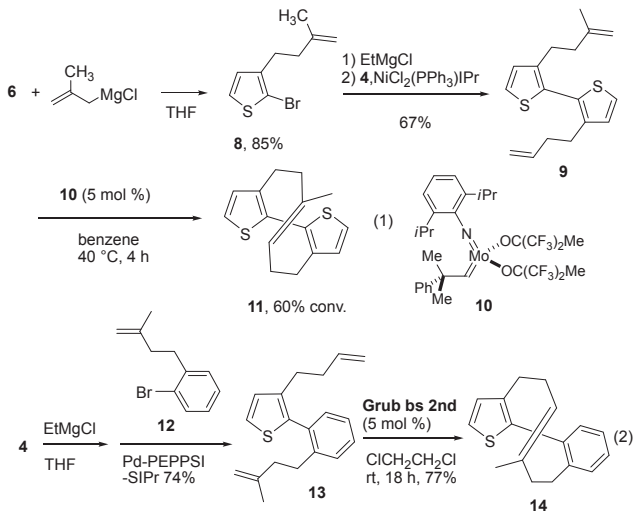


Figure 1. (a) HPLC profile of **7** with chiral column (DAICEL Chiralpak IF) and (b) X-ray crystal structure of the cyclized product **7**.

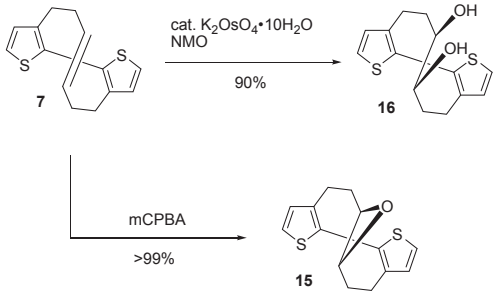


Scheme 3. Preparation of metathesis precursors and ring-closing metathesis of unsymmetrical (hetero)biaryls.

whereas the nitrogen of imidazole, showing slightly sp^3-like characteristics,[4] resulted in the smaller angle.

We next envisaged unsymmetrical (hetero)biaryl derivatives. Metathesis precursor of bithiophene bearing a different substituent in the side chain was synthesized as shown in Scheme 3 (1). The reaction of bromomethyl-bromothiophene **6** with methallyl Grignard reagent afforded **8** in 85% yield. Following halogen metal exchange with EtMgCl and the reaction of bromothiophene bearing a 3-butenyl substituent furnished the corresponding unsymmetrical bithiophene **9** in 67% yield. Although RCM of bithiophene with an unsymmetrical substituent leading to trisubstituted olefin **11** was found unsuccessful with a ruthenium catalyst, the reaction was found to proceed using Schrock's molybdenum-alkylidene catalyst **10**[16] to afford the cyclized bithiophene **11** (60% conversion). The metathesis precursor bearing thiophene and benzene rings was also synthesized as shown in Scheme 3 (2) by the reaction of bromothiophene **4** with EtMgCl followed by treatment with bromobenzene **12**, which was prepared by the reaction of 2-bromomethyl-bromobenzene with methallyl Grignard reagent, in the presence of Pd-PEPPSI-SIPr as a catalyst to afford **13** in 74% yield. RCM of **13** was found to proceed successfully with Grubbs 2nd generation catalyst (5 mol %) in 77% yield.

Transformation reactions of the *E*-olefin in the macrocyclic bithiophene were examined. As revealed in our previous



Scheme 4. Transformation of the olefin moiety of bithiophene **7**.

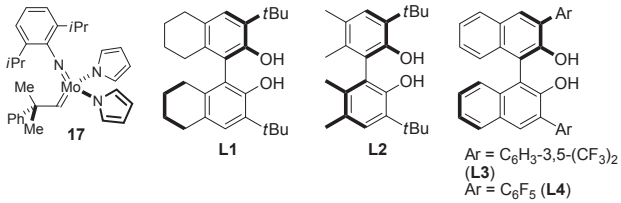
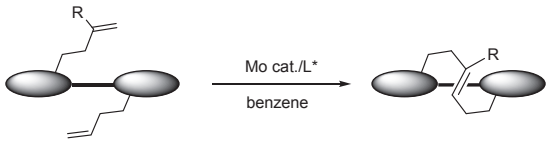


Chart 1. Molybdenum-alkylidene precursor **17** and chiral ligands **L**.

studies on the transformation of vine-shaped bisimidazoles,[4b] several reactions shown to proceed in a cis-addition manner were found to take place smoothly. Epoxidation proceeded with *m*CPBA to afford the corresponding epoxide **15** in a quantitative yield. The reaction of **7** with catalytic osmium/NMO also afforded the dihydroxylation product **16** (90%). The obtained epoxide and diol involve formation of diastereomers, however, HPLC and NMR analyses of **15** and **16** only revealed the single isomers suggesting that the reactions proceeded in diastereoselective manner (Scheme 4).

Enantioselective RCM of bithiophene derivative was studied with a molybdenum-alkylidene complex in the presence of a chiral ligand composed of axially chiral biphenol or binaphthol derivatives.[5,17] The reaction was carried out with bithiophene **1** with 10 mol % Mo precursor **17** and 10 mol % chiral ligand **L** (Chart 1), which were mixed to generate the chiral complex in situ, in a benzene solution.[18,19] Several chiral ligands were examined, however, asymmetric induction was not observed in the RCM reaction with **L1**–**L3** as a ligand whereas the reaction proceeded smoothly. When **9** with unsymmetrical-structure-forming trisubstituted olefin **11** was employed as a metathesis precursor, a good enantioselectivity was observed albeit with much lower conversion with Mo/**L1** catalyst (82% ee, 14% conv.). The yield of the RCM product was improved with chiral ligand **L3** or **L4** (78% and 77% yields, respectively) with slightly inferior selectivities (42% ee and 61% ee). It is interesting to compare the observed selectivity in ARCM with asymmetric synthesis of planer-chiral cyclic amide by palladium-catalyzed allylic substitution shown by Tomooka and co-workers,[20] in which the presence of a substituent at the olefinic moiety plays a significant role to show excellent asymmetric induction. It was also found that biaryl composed of thiophene and benzene **13** effected the reaction to afford the metathesis product **14** in an excellent enantioselectivity with **L3** (67% ee) and **L4** (87% ee). These results are summarized in Table 2.

Table 2. Ring-closing metathesis of bithiophene 1[a)]



Substrate	Ligand	Product	Conv. (%)[b)]	%ee[c)]
1	**L1**	**7**	81	0
(R=H)	**L2**		86	0
	L3		86	0
9	**L1**	**11**	14	82
($R=CH_3$)	**L3**		78	42
	L4		77	61
13	**L3**	**14**	71	67
($R=CH_3$)	**L4**		67	87

a) The reaction of substrate (0.1 mmol) was carried out for 12 h in anhydrous benzene (2 mL) in the presence of 10 mol % molybdenum complex **17** and 10 mol % chiral ligand. b) The conversion was determined by ^{1}H NMR analysis of the crude mixture. c) Enantiomeric excess was determined by HPLC bearing a chiral stationary phase column Daicel Chiralpak IC.

3. Conclusion

In summary, we have shown that bithiophene derivatives with winding vine-shaped molecular asymmetry are synthesized by ring-closing metathesis catalyzed by a ruthenium or molybdenum complex. The obtained bithiophene was confirmed to be separated by HPLC with a chiral column and X-ray crystal structure analysis of **7** revealed the selective formation of *E*-alkene and the dihedral angle between thiophene–thiophene bond was 74°, which was larger than that of the related bisimidazole (48°). Asymmetric metathesis (ARCM) was found to proceed in the reaction of unsymmetrical substrate, which lead to trisubstituted olefin, with chiral molybdenum catalyst in moderate to good enantioselectivities albeit the determination of the absolute configuration has not been successful yet.

4. Experimental

General. All the reactions were carried out with standard Schlenk technique under nitrogen atmosphere unless otherwise noted. Asymmetric ring-closing metathesis (ARCM) was carried out in a glove box and anhydrous benzene employed for the reaction was freshly distilled prior to use. X-ray structure analysis was performed with a Rigaku Saturn CCD area detector with graphite monochromated Mo Kα radiation at the Japan Atomic Energy Agency. High resolution mass spectra (HRMS) were measured with a JEOL JMS-T100LP AccuTOF LC-Plus (ESI) with a JEOL MS-5414DART attachment. HPLC analyses with a chiral column was carried out with a JASCO LC-2000 Plus with chiral column Daicel Chiralpak IF or IC (0.46 cm I.D. × 25 cm, flow rate: 1.0 mL/min) using a UV (297 nm) detector. Benzene was distilled from sodium benzophenone ketyl prior to use. Unless otherwise specified, other chemicals were purchased and used as such.

3-(3-Oxo-propan-1-yl)thiophene (3): A mixture of thiophene-3-boronic acid pinacol ester (**2**, 6.0 g, 29 mmol), acrolein (1.23 g, 22 mmol), $[Rh(OH)cod]_2$ (200 mg, 0.6 mmol), xantphos (380 mg, 0.9 mmol) was prepared. The mixture was dissolved in methanol (5.5 mL), water (5.5 mL), and toluene (110 mL), and was stirred at 50 °C under nitrogen atmosphere. After cooling to room temperature, the reaction mixture was poured into water and the organic phase was separated. The aqueous phase was extracted with diethyl ether. The combined organic layer was washed with water twice and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to leave a crude oil, which was subjected to silica-gel chromatography to afford **3** (2.8 g, 91%), which was identical with the authentic sample and employed directly for the next reaction without further purification.[9a]

2-Bromo-3-(3-buten-1-yl)thiophene (4): To a solution of **3** (1.0 g, 7.2 mmol) in 30 mL THF was added *N*-bromosuccinimide (1.28 g, 7.2 mmol) in five portions with 1 h interval at 0 °C under nitrogen atmosphere. After completion of the reaction was confirmed, the resulting mixture was poured into water to result in phase separation. The aqueous layer was extracted with diethyl ether twice and the combined organic layer was dried over anhydrous sodium sulfate. After removal of the solvent, the obtained crude oil was passed through a silica-gel column using hexane/ethyl acetate as an eluent to afford 1.41 g of the corresponding bromide (90%), which was employed for the following reaction. A solution of methyl(triphenyl)phosphonium iodide (3.1 g, 7.8 mmol) in THF (70 mL) was cooled to −78 °C under nitrogen atmosphere. An equimolar amount of *n*BuLi (1.6 M hexane solution) was added to the solution dropwise and further stirring was continued for 3 h. To the resulting mixture was added the obtained bromothiophene (1.4 g, 6.5 mmol) at −78 °C. The mixture was gradually warmed to room temperature and stirring was further continued for 20 h. The mixture was poured into water to result in phase separation. The aqueous layer was extracted with diethyl ether twice and the combined organic layer was dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to leave a crude oil, which was purified by column chromatography on silica gel using hexanes as an eluent to afford 0.77 g of **4**, which was identical with the authentic sample (55%).[10]

Preparation of 2-bromo-3-(3-buten-1-yl)thiophene (**4**) was also carried out with 3-methylthiophene (**5**) by sequential ionic and radical bromination with NBS and NBS/AIBN to give 2-bromo-3-bromomethyl-thiophene (**6**) and treatment with allylmagnesium chloride to give **4** was performed in a manner reported previously.[10]

2-[(3-Buten-1-yl)thiophene-2-yl]-3-(3-buten-1-yl)thiophene (1): To a 50 mL Schlenk tube equipped with a magnetic stirring bar was dissolved 2-bromo-3-(3-buten-1-yl)-thiophene (**4**) (2.16 g, 10.0 mmol) in 15 mL THF under N_2, Ethylmagnesium chloride (0.95 M THF solution: 5.26 mL, 5.0 mmol) was added dropwise and stirring was continued at room temperature for 2 h. $NiCl_2(PPh_3)IPr$ (78 mg, 0.1 mmol) was added to the resulting mixture, which was stirred at 60 °C for 20 h. After cooling to room temperature, the mixture was poured into water to separate into two phases. The aqueous layer was extracted with diethyl ether. The combined organic layer was washed with water twice and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to leave a crude oil, which was purified by chromatography on silica gel using hexane as an eluent to afford 0.85 g of **1** as a colorless liquid

(63% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.29 (dt, $J = 2.3$, 7.2 Hz, 4H), 2.61 (t, $J = 8.7$ Hz, 4H), 4.93 (d, $J = 11.5$ Hz, 2H), 4.98 (d, $J = 17.1$ Hz, 2H), 5.71–5.85 (m, 2H), 6.98 (d, $J =$ 5.2 Hz, 2H), 7.29 (d, $J = 5.2$ Hz, 2H); ^{13}C NMR δ 28.34, 34.76, 115.08, 125.55, 128.56, 129.02, 137.96, 141.38; IR (ATR) 3076, 2922, 2851, 1640, 1448, 1412, 1232, 1089, 994, 912, 831, 724 cm^{-1}; HRMS (DART-ESI+) Calcd for $C_{16}H_{19}S_2$ $[M+H]^+$: 275.0928; found: m/z 275.0939.

Cyclodeca[2,1-*b*:3,4-*b*′]dithieno-7-(*E*)-ene (7): To a solution of 3,3′-bis(3-buten-1-yl)-2,2′-bithiophene (**4**) (1.01 g, 3.7 mmol) in 150 mL of dichloromethane was added Grubbs 1st generation catalyst (0.30 g, 0.37 mmol) under nitrogen atmosphere and stirring was continued at room temperature for 5 h. The solvent was removed under reduced pressure to leave a crude solid, which was purified by chromatography on silica gel using hexanes as an eluent to afford 0.80 g of **7** as a colorless solid. (88% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.62–1.74 (m, 2H), 2.27–2.35 (m, 2H), 2.50 (td, $J = 13.1$, 2.8 Hz, 2H), 2.75 (ddd, $J = 13.1$, 4.6, 2.8 Hz, 2H), 4.37–4.52 (m, 2H), 6.89 (d, $J = 5.2$ Hz, 2H), 7.26 (d, $J = 5.2$ Hz, 2H); ^{13}C NMR δ 28.50, 34.23, 124.90, 129.48, 129.83, 131.54, 140.92; IR (ATR) 2925, 2854, 1457, 1439, 1227, 1185, 1053, 969, 877, 827, 726, 657 cm^{-1}; HRMS (DART-ESI+) Calcd for $C_{14}H_{15}S_2$ $[M+H]^+$: 247.0615; found: m/z 247.0610.

Preparation of 1 by Oxidative Homocoupling with $CuCl_2$: To a solution of **4** (130 mg, 0.6 mmol) was added EtMgCl (0.93 M THF solution, 0.77 mL, 0.72 mmol) dropwise and the resulting solution was stirred at 60 °C for 3 h. $CuCl_2 \cdot 2H_2O$ (102 mg, 0.6 mmol), THF (2 mL) and TMEDA (0.09 mL, 0.6 mmol) were then added to the mixture and further stirring was continued at 60 °C for 20 h. After cooling to room temperature, the mixture was passed through a celite pad, which was washed with chloroform repeatedly. The filtrate was poured into water and the aqueous layer was extracted with diethyl ether. The combined organic layer was washed with water twice and dried over anhydrous sodium sulfate. Removal of the solvent left a crude oil, which was purified by column chromatography on silica gel using hexanes as an eluent to afford 50 mg of **1** (70%).

3-(3-Buten-1-yl)-3′-(3-methyl-3-buten-1-yl)-2,2′-bithiophene (9): Preparation of **9** was carried out with **4** and **8** (0.67 g, 1.7 mmol), which was prepared by the reaction of **6** and methallymagnesium chloride, in a similar manner to that of **4** to afford 0.33 g of **9** as a colorless liquid (67% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.70 (s, 3H), 2.25–2.38 (m, 4H), 2.63–2.73 (m, 4H), 4.70 (d, $J = 22.7$ Hz, 2H), 4.96 (d, $J = 10.3$ Hz, 1H), 5.02 (d, $J = 17.1$ Hz, 1H), 5.81 (ddt, $J = 17.1$, 10.3, 6.5 Hz, 1H), 7.00 (d, $J = 5.2$ Hz, 2H), 7.29 (d, $J = 5.2$ Hz, 2H); ^{13}C NMR δ 22.53, 27.30, 28.34, 34.79, 38.77, 110.43, 115.07, 125.54, 125.55, 128.55, 128.56, 128.89, 129.02, 137.99, 141.34, 141.63, 145.13; IR (ATR) 3073, 2925, 2853, 1649, 1448, 1374, 1231, 1091, 995, 912, 829, 723, 647 cm^{-1}; HRMS (DART-ESI+) Calcd for $C_{17}H_{21}S_2$ $[M+H]^+$: 289.1085; found: m/z 289.1086.

2-[3-(3-Buten-1-yl)thiophene-2-yl]-1-(3-methyl-3-buten-1-yl)benzene (13): Preparation of **13** with **4** (0.43 g, 2 mmol) and 2-bromo-1-(3-methyl-3-buten-1-yl)benzene (**12**, 0.50 g, 2.2 mmol), which was prepared by the reaction of 1-bromo-2-(bromomethyl)benzene and methallymagnesium chloride, was carried out in a similar manner to that of **4** to afford 0.41 g of **13** (74%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.62 (s, 3H), 2.13–2.31 (m, 4H), 2.47 (dd, $J = 9.5$, 8.5 Hz, 2H), 2.60–2.70 (m, 2H), 4.62 (d, $J = 17.1$, 2H), 4.90 (d, 10.2 Hz, 1H), 4.94 (d, 16.2 Hz, 1H), 5.74 (ddt, $J = 17.1$, 10.2, 6.6 Hz, 1H), 6.98 (d, $J = 5.13$ Hz, 1H), 7.26 (d, $J = 5.2$ Hz, 1H), 7.20–7.24 (m, 1H), 7.26 (d, $J = 5.2$ Hz, 1H), 7.28–7.33 (m, 2H); ^{13}C NMR δ 22.44, 28.22, 32.03, 34.72, 39.46, 110.27, 115.03, 123.94, 125.68, 128.07, 128.46, 129.16, 132.02, 133.39, 126.68, 138.13, 138.65, 142.29, 145.49; IR (ATR) 3071, 2967, 2933, 2852, 1948, 1450, 912, 889, 835, 756, 723, 647 cm^{-1}; HRMS (DART-ESI+) Calcd for $C_{19}H_{23}S_1$ $[M+H]^+$: 283.1521; found: m/z 283.1514. The product contains a trace amount of inseparable impurities despite attempted purifications. Thus, crude **13** was employed for the metathesis reaction.

Ring-closing-metathesis reactions with a ruthenium catalyst were carried out in a similar manner to that forming **7**. The reaction with a molybdenum catalyst was carried out in a glove box with the metathesis precursor (0.1 mmol) and (2,6-iPr$_2$-C_6H_3)N=Mo(=CHCPhMe$_2$)[OC(CF$_3$)$_2$Me]$_2$, (10 mol %) in anhydrous benzene (2 mL). The conversion was monitored by measurement of ^{1}H NMR spectrum. Spectroscopic characterization and analytical data are shown below.

7-Methyl-cyclodeca[2,1-*b*:3,4-*b*′]dithieno-7-(*E*)-ene (11): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (s, 3H), 1.84 (td, $J =$ 11.9, 3.7 Hz, 1H), 2.00–2.15 (m, 2H), 2.21 (ddd, $J = 12.1$, 3.6 Hz, 1H), 2.54 (td, $J = 12.8$, 3.9 Hz, 1H), 2.67–2.78 (m, 2H), 2.81 (dt, $J = 13.0$, 3.6 Hz, 1H), 4.23 (dd, $J = 10.7$, 4.7 Hz, 1H), 6.90 (d, $J = 5.1$ Hz, 1H), 6.92 (d, $J = 5.1$ Hz, 1H), 7.23 (d, $J = 5.1$ Hz, 1H), 7.27 (d, $J = 5.1$ Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.18, 27.12, 28.42, 29.51, 41.84, 123.63, 124.95, 125.14, 129.84, 130.00, 131.19, 131.48, 134.01, 141.36, 141.83; IR (ATR) 2924, 2857, 1444, 1408, 1383, 1233, 1193, 1088, 1067, 1016, 998, 878, 834, 817, 772, 725, 691, 675, 656, 645 cm^{-1}; HRMS (DART-ESI+) Calcd for $C_{15}H_{17}S_2$ $[M+H]^+$: 261.0784; found: m/z 261.0772.

7-Methyl-cyclodeca[2,1-*b*]thieno-[3,4]benzo-7-(*E*)-ene (14): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (s, 3H), 1.88 (td, $J = 12.3$, 2.4 Hz, 1H), 2.01–2.10 (m, 2H), 2.25–2.38 (m, 2H), 2.64 (ddd, $J = 12.6$, 5.3, 2.3 Hz, 1H), 2.76 (dt, $J = 12.9$, 3.5 Hz, 1H), 3.07 (td, $J = 128$, 2.2 Hz, 1H), 4.09–4.19 (m, 1H), 6.92 (d, $J = 5.1$, 1H), 7.07 (dd, $J = 7.5$, 1.3, 1H), 7.18 (d, $J =$ 5.1 Hz, 1H), 7.18–7.33 (m, 4H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 14.63, 28.38, 29.52, 32.03, 43.04, 122.44, 123.46, 125.97, 128.37, 129.97, 131.11, 131.75, 134.65, 136.28, 138.14, 139.82, 142.93. IR (ATR) 3060, 2925, 2859, 1483, 1447, 1382, 1233, 1106, 1016, 1016, 967, 878, 838, 754, 721, 660, 646, 589 cm^{-1}; HRMS (DART-ESI+) Calcd for $C_{17}H_{19}S$ $[M+H]^+$: 255.1208; found: m/z 255.1211.

Epoxidation of Macrocyclic Alkene 7: To a solution of **7** (24.6 mg, 0.1 mmol) in 1 mL of $CHCl_3$ and 1 mL of saturated $NaHCO_3$ aq. was added *m*-chloroperbenzoic acid (51.7 mg, 0.3 mmol) at room temperature. The resulting mixture was allowed to stir at 60 °C for 2 h. The reaction mixture was poured into water and two phases were separated. The aqueous phase was extracted twice with $CHCl_3$ and the combined organic layer was dried over anhydrous sodium sulfate. The organic layer was washed with water twice and dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure left a

crude solid, which was purified by column chromatography on silica gel using hexane/isopropyl acetate (10:1) as an eluent to afford 27.4 mg of epoxide **15** as a colorless solid (>99% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88–1.02 (m, 2H), 2.00 (dt, J = 11.6, 2.2 Hz, 2H), 2.26–2.36 (m, 2H), 2.69–2.87 (m, 4H), 6.91 (d, J = 5.2 Hz, 2H), 7.31 (d, J = 5.2 Hz, 2H). ^{13}C NMR δ 24.16, 33.94, 57.94, 126.04, 129.33, 129.63, 142.35; IR (ATR) 2963, 2923, 2856, 1469, 1444, 1413, 1236, 1215, 1093, 1042, 1023, 984, 906, 863, 854, 822, 797, 782, 732, 691, 677, 660 cm^{-1}; HRMS (DART-ESI+) Calcd for $C_{14}H_{15}S_2O$ $[M+H]^+$: 263.0564; found: m/z 263.0572.

Dihydroxylation of Macrocyclic Alkene 7: To a solution of **7** (24.6 mg, 0.1 mmol) in 1 mL of acetone and 0.5 mL of water was added OsO_4 (1.6 mg, 0.005 mmol) and *N*-methylmorpholine-*N*-oxide (20 µL, 0.12 mmol) at room temperature. The resulting mixture was allowed to stir at room temperature for 1 week. The reaction mixture was poured into water and two phases were separated. The aqueous phase was extracted twice with $CHCl_3$. The organic layer was washed with water twice and dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure left a crude solid, which was purified by column chromatography on silica gel using hexane/isopropyl acetate (50:50–0:100) as an eluent to afford 31 mg of diol **16** as a colorless solid (90% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.70–1.82 (m, 4H), 1.95 (brs, 2H), 2.33–2.44 (m, 2H), 2.68 (dt, J = 14.3, 4.2 Hz, 2H), 3.39 (brs, 2H), 6.95 (d, J = 5.2 Hz, 2H), 7.36 (d, J = 5.2 Hz, 2H); ^{13}C NMR δ 24.31, 33.43, 66.47, 127.14, 127.87, 129.10, 142.39; IR (ATR) 3384, 2923, 1445, 1157, 1069, 999, 979, 886, 833, 729, 679, 647 cm^{-1}; HRMS (DART-ESI+) Calcd for $C_{14}H_{17}S_2O_2$ $[M+H]^+$: 281.0670; found: m/z 281.0666.

Typical Procedure for Enantioselective RCM Catalyzed by Chiral Molybdenum Carbene Complex 17 Representative as the Case of L1: Molybdenum complex **17** (3.1 mg, 0.0058 mmol) was dissolved in 1.0 mL anhydrous benzene in a 10 mL screw-capped test tube equiped with a magnetic stirring bar in a glove box. To the resulting solution was added chiral ligand **L1** (2.4 mg, 0.0058 mmol) and further stirring was continued at room temperature for 0.5 h followed by addition of metathesis precursor (0.1 mmol). The reaction mixture was stirred at room temperature for 12 h. The test tube was taken out of the glove box and acetone (2.0 mL) was added to quench the reaction. The mixture was passed through a short path silica-gel column. The solution was concentrated under reduced pressure to leave an oil, which was subjected to measurement of ^{1}H NMR spectrum to estimate conversion. The enantioselectivity was measured by HPLC analysis with a chiral column (Daicel Chiralpak IC or IF) using hexane as an eluent.

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Supporting Information

Spectroscopic and analytical data. This material is available on http://dx.doi.org/10.1246/bcsj.20160265.

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